cyclopentane ring (cyclopentenone PG, cyPG) have been shown *in vitro* to have the interesting ability to interfere with virus replication at multiple levels (Santoro et al., 1997, Trends Microbiol. 5: 276-281). For example, prostaglandins of the A and J type (PGAs and PGJs) have been shown to inhibit the replication of a variety of RNA viruses, including paramyxoviruses, rhabdoviruses, rotaviruses and retroviruses in cultured cells (reviewed in Santoro et al., 1997, *supra*).

On page 3, please replace the paragraph beginning on line 13 with the following paragraph:

The inactive form of NF-κB is localized in the cytoplasm, and upon activation by a variety of agents (*e.g.*, cytokines, oxygen free radicals, inhaled particles, ultraviolet light, bacterial products, and viral products) is translocated to the nucleus. NF-κB is tightly associated with a class of specific inhibitory proteins, called IκBs, that prevent the translocation and DNA binding of the transcription factor (see, *e.g.*, Chen et al., 1999, Clinical Chemistry 45:7-17 and Baeuerle, 1998, Cell 95:729-731). In response to a variety of agents, IκB is phosphorylated in its N-terminal domain by a large multikinase complex, polyubiquitinylated, and degraded by the proteasome (see, *e.g.*, Baeuerle, 1998, Curr. Biol. 8:R19-R22; Ghosh et al., 1998, Annu. Rev. Immunol. 16:225-260). Once NF-κB is dissociated from IκB, it translocates to the nucleus and initiates the transcription of genes by binding to its cognate DNA motifs in the regulatory segments of genes. The active form of NF-κB induces the transcription of a variety of genes encoding proteins involved in controlling the immune and inflammatory responses, including genes encoding cytokines (*e.g.*, interleukins and tumor necrosis factor alpha), NO synthase, cyclo-oxygenase-2, chemokines, growth factors, cell adhesion factors and acute phase proteins.

On page 3, please replace the paragraph beginning on line 28 with the following paragraph:

NF-κB is an early mediator of the immune and inflammatory responses, and it is involved in the control of cell proliferation and in the pathogenesis of various human diseases, including, but not limited to, rheumatoid arthritis (Beker et al., 1995, Clin. Exp. Immunol. 99: 325), ischemia (Salminen et al., 1995, Biochem. Biophys. Res. Comm. 212:

939), arteriosclerosis (Baldwin et al., 1996, Annals Rev. Immunol. 14: 649), autoimmune arthritis, asthma, septic shock, lung fibrosis, glomerular nephritis, and acquired immunodeficiency syndrome (AIDS). Many viruses, including human immunodeficiency virus-1 (HIV-1) and human T-cell leukemia virus type I (HTLV-1), utilize NF-κB to their transcriptional advantage during infection. For example, the transcription of HIV-1 virus RNAs by NF-κB is caused by the presence of κB-sites in the (LTR) (Long Terminal Repeats) sequences of the virus genome (Baltimore et al., 1989, Cell 58: 227-229). Thereforeh, the discovery of compounds that downregulate or inhibit NF-κB activation after administration to humans would be beneficial for the treatment of diseases and/or disorders associated with inappropriate or aberrant NF-κB activity.

On page 10, please replace the paragraph beginning on line 14 with the following paragraph:

Efficacy in treating or preventing viral infection may be demonstrated by detecting the ability of the cyclopentenone compound or derivative thereof to inhibit the replication of the virus, to inhibit transmission or prevent the virus from establishing itself in its host, or to prevent, ameliorate or alleviate the symptoms of disease progression. The treatment is considered therapeutic if there is, for example, a reduction in viral load, amelioration of one or more symptoms, or a decrease in mortality and/or morbidity following administration of the compounds of the invention.

On page 11, please replace the paragraph beginning on line 10 with the following paragraph:

It has been discovered that compounds with an α,β- unsaturated ketone ("enone") moiety are the preferred compounds of the invention. The enone moiety may be present in a ring or in an acyclic structure, for example, cyclopentenone, cyclohexenone, cycloheptone and the like or simple acyclic α,β- unsaturated carbon chains may be used. The preferred compounds of the present invention comprise compounds with a cyclopentenone ring structure. The cyclopentenone containing compounds may or may not contain long aliphatic lateral side chains similar to those present in prostaglandins or punaglandins that have a cyclopentenone ring structure (sometimes referred to as a cyclopentenone nucleus).

Accordingly, the compounds may lack one or more long aliphatic lateral side chains at the 4 and/or 5 positions of the cyclopentenone ring.

On page 14, please replace the paragraph beginning on line 6 with the following paragraph:

In a preferred embodiment, therapeutic methods and pharmaceutical compositions for treating, inhibiting or preventing infectious diseases, immune disorders, cancer, ischemia, arteriosclerosis and diabetes in animals, comprise 2-cyclopenten-1-one or a derivative of 2-cyclopenten-1-one.

On page 14, please replace the paragraph beginning on line 16 with the following paragraph:

In a preferred embodiment, therapeutic or pharmaceutical compositions are administered to an animal to treat, prevent or inhibit infectious diseases. Infectious diseases include diseases associated with yeast, fungal, viral and bacterial infections. Viruses causing viral infections which can be treated or prevented in accordance with this invention include, but are not limited to, retroviruses (*e.g.*, human T-cell lymphotrophic virus (HTLV) types I and II and human immunodeficiency virus (HIV)), herpes viruses (*e.g.* , herpes simplex virus (HSV) types I and II, Epstein-Barr virus, HHV6-HHV8, and cytomegalovirus), arenavirues (*e.g.*, lassa fever virus), paramyxoviruses (*e.g.*, morbillivirus virus, human respiratory syncytial virus, mumps, and pneumovirus), adenoviruses, bunyaviruses (*e.g.*, hantavirus), coronaviruses, filoviruses (*e.g.*, Ebola virus), flaviviruses (*e.g.*, hepatitis C virus (HCV), yellow fever virus, and Japanese encephalitis virus), hepadnaviruses (*e.g.*, hepatitis B viruses (HBV)), orthomyxoviruses (*e.g.*, influenza viruses A, B and C), papovaviruses (*e.g.*, papillomaviruses), picornaviruses (*e.g.*, rhinoviruses, enteroviruses and hepatitis A viruses), poxviruses, reoviruses (*e.g.*, rotaviruses), togaviruses (*e.g.*, rubella virus), and rhabdoviruses (*e.g.*, rabies virus). Microbial pathogens causing bacterial infections include, but are not limited to, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Neisseria gonorrhoea*, *Neisseria meningitidis* , *Corynebacterium diphtheriae* , *Clostridium botulinum*, *Clostridium perfringens*, *Clostridium tetani*, *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Klebsiella ozaenae*, *Klebsiella rhinoscleromotis*, *Staphylococcus aureus*, *Vibrio cholerae*, *Escherichia*

coli, *Pseudomonas aeruginosa*, *Campylobacter* (Vibrio) *fetus*, *Campylobacter jejuni*, *Aeromonas hydrophila*, *Bacillus cereus*, *Edwardsiella tarda*, *Yersinia enterocolitica*, *Yersinia pestis*, *Yersinia pseudotuberculosis*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Salmonella typhimurium*, *Treponema pallidum*, *Treponema pertenue*, *Treponema carateneum*, *Borrelia vincentii*, *Borrelia burgdorferi*, *Leptospira icterohemorrhagiae*, *Mycobacterium tuberculosis*, *Toxoplasma gondii*, *Pneumocystis carinii*, *Francisella tularensis*, *Brucella abortus*, *Brucella suis*, *Brucella melitensis*, *Mycoplasma spp.*, *Rickettsia prowazeki*, *Rickettsia tsutsugumushi*, *Chlamydia spp.*, and *Helicobacter pylori*.

On page 17, please replace the paragraph beginning on line 30 with the following paragraph:

Efficacy in treating or preventing viral infection may be demonstrated by detecting the ability of the cyclopentenone compound to inhibit the replication of the virus, to inhibit transmission or prevent the virus from establishing itself in its host, or to prevent, ameliorate or alleviate the symptoms of disease progression. The treatment is considered therapeutic if there is, for example, a reduction in viral load, amelioration of one or more symptoms or a decrease in mortality and/or morbidity following administration of a compound of the invention.

On page 24, please replace the paragraph beginning on line 31 with the following paragraph:

In one embodiment, agents that induce one or more heat shock proteins and/or downregulate or inhibit NF-κB activity are identified in a cell-based assay system. In accordance with this embodiment, cells are contacted with a candidate compound (*e.g.*, 2-cyclopenten-1-one) or a control compound (*e.g.*, phosphate buffered saline (PBS)) and the ability of the candidate compound to induce one or more heat shock proteins and/or downregulate or inhibit NF-κB activity is determined. The level of expression of one or more heat shock proteins or the downregulation of NF-κB activity in the presence of the candidate compound is compared to the level of expression of one or more heat shock proteins or the downregulation of NF-κB activity in the absence of the candidate compound (*e.g.*, in the presence of a control compound). The candidate compound can then be identified based on